

REMARKS

Claims 10-11, 179, 181-182, and 187-209 are pending. Claims 10-11, 178, 181-182, and 187-209 were rejected. Claims 10, 11, 179, 181-182, 189-190, and 209 have been amended. Accordingly, claims 10-11, 179, 181-182, and 187-209 are currently under consideration.

Amendments

Claims 10, 11, 179, 181-182, 189-190, and 209 have been amended. Support for the amendments of claims 10, 181-182, 189, and 209 is found, *inter alia*, at page 77, lines 15-23, page 79, lines 13-21, page 80, lines 16-24, page 91, lines 10-12, page 94, lines 4-33, and page 96, line 31 – page 97, line 25. Support for the amendments of claim 11 is found, *inter alia*, at page 77, lines 15-23, page 91, lines 10-12, and page 94, lines 4-33. Claims 179 and 190 have been amended to clarify the scope of the claim.

With respect to all amendment to claims, Applicants have not dedicated or abandoned any unclaimed subject matter and, moreover, have not acquiesced to any rejections and/or objections made by the Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation, continuation-in-part, and/or divisional applications.

Claim Objections

Claims 10-11, 179, 189-190, and 209 have been objected to as reciting alternative terminology for the term FGF19. The Examiner noted that claims 10, 11, 189, and 209 recite “FGF19” while claims 179 and 190 recite “FGF-19.”

Applicants have amended claims 179 and 190 to recite the term “FGF19.”

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the objection to claims 10-11, 179, 189-190, and 209.

Claim Rejections – 35 U.S.C. § 112

Claims 10-11, 181-182, 189, 209, and their dependent claims are rejected under 35 U.S.C. §112, second paragraph, as being indefinite or failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicants respectfully traverse.

The Examiner alleges at page 3 of the Office Action dated 10/10/08 that claims 10, 11, 181, 189 and 209 are indefinite as they recite “the control ... transgenic mouse” as a control for a testing carried out on “a transgenic mouse.” The Examiner states that the Applicants should describe the appropriate conditions under which said transgenic mouse acts as a control and recommended amending the claims to recite that “said transgenic mouse that is untreated with said compound etc., acts as a control.”

Applicants respectfully disagree and submit that a person skilled in the art would clearly understand the meaning of the phrase “the control ... transgenic mouse.” Solely to expedite prosecution and without acquiescing to the correctness of the Examiner’s argument, Applicants have amended claims 10, 181-182, 189, and 209 to recite “a control transgenic mouse that is untreated with said candidate agent.” Applicants have deleted the phrase “or transgenic” from claim 11.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 10-11, 181-182, 189, 209, and their dependents under 35 U.S.C. § 112, second paragraph.

Claim Rejections – 35 U.S.C. § 112

Claims 10, 11, 189, 209, and their dependent claims 179, 181-182, 187-188, and 190-208 stand rejected under 35 U.S.C. § 112, first paragraph, as not being enabled. Applicants respectfully traverse.

The Examiner alleges that, while being enabling for a FGF19 transgenic mouse wherein said transgene is expressed under the control of a promoter in a skeletal muscle cell and wherein said transgenic mouse has a phenotype of developing hepatocellular carcinoma (HCC), the specification is not enabled for a HCC mouse wherein the FGF19 gene is not expressed or expressed under any cell or tissue. The Examiner further alleges that the Applicant’s arguments taken from the art

regarding expression of an unrelated gene (growth hormone) using distinct promoters do not suffice to support enablement of the pending claims.

The Applicants respectfully disagree. The Examiner has failed to establish a *prima facie* case of enablement. The Examiner has not established that the disclosure of the specification lacked sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. *See* MPEP § 2164.01. The Applicants have submitted, in addition to the MCL promoter disclosed in the specification, additional references indicating that one of skill in the art would have been aware of numerous promoter systems that would be suitable for expression of a secreted small protein such as FGF19 from a transgene as of the priority date of the application. The Examiner simply alleges, without pointing to any evidence, that art regarding expression of an unrelated gene (growth hormone) using distinct promoters does not suffice to support enablement of the pending claims.

Further, the Examiner alleges that the claims do not indicate that FGF19 gene is expressed or that FGF19 expression is needed for the induction of the hepatocellular carcinoma phenotype in the mouse.

Applicants submit that one of skill in the art would know that in order to practice the claimed method of screening recited in claims 10, 11, 189, and 209 the transgenic mouse must comprise an integrated transgene encoding FGF19 operably linked to a promoter, wherein said transgene expresses FGF19 and FGF19 expression in a manner that results in hepatocellular carcinoma in the liver. The specification provides ample guidance as to the detection of hepatocellular carcinoma in the transgenic mice. *See* specification at p. 94, *inter alia*.

The specification states that the transgenic mouse expresses FGF19 in muscle and hepatocellular carcinoma is induced in the liver. ("To understand in vitro effects of FGF19, transgenic mice over-expressing FGF19 in skeletal muscle were generated. By 10 months of age, hepatocellular carcinoma (HCC) developed in the FGF19 transgenic mice." Specification at Example 8, page 90, first full paragraph. The instant invention, for the first time, shows ectopic expression of an oncogene leading to hepatic cancer. *See* specification at page 90, lines 18-19. As described in the specification, FGF-19 is expressed in the skeletal muscle (*see* specification at page

90), secreted in the serum (*see* specification at pages 91-92 and 94) and acts on the liver to induce hepatocellular carcinoma (*see* specification at page 94).

Solely to expedite prosecution and without acquiescing to the correctness of the Examiner's statements, the Applicants have amended claims 10, 11, 189, and 209 to recite "a stably integrated transgene encoding FGF19 operably linked to a promoter, wherein said transgene expresses FGF19 under control of the promoter in a skeletal muscle cell" as suggested by the Examiner and indicated on page 3 of the Office Action dated 10/10/2008 as enabled.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 10, 11, 189, and 209 and their dependent claims 179, 181-182, 187-188, and 190-208 under 35 U.S.C. § 112, first paragraph.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 146392001900. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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